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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,170	11/10/2000	Raymond P. Warrell	10412-025	4982

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
03/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/709,170	WARRELL ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 7-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, and 7-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed December 17, 2007.

Claims 1, 3-5, 7-10, 12-16, and 19 have been amended.

Claims 1, 3-5, and 7-23 are pending in the instant application.

Claims 1, 3-5, and 7-23 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed August 22, 2007, claims 1, 3-5, and 7-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (The Lancet, 1997 Vol. 349:1137-1141, Applicant's reference CP on the Information Disclosure Statement filed February 23, 2001), in view of Waters et al. (Journal of Clinical Oncology, 2000 Vol. 18:1812-1823, Applicant's reference CO on the Information Disclosure Statement filed February 23, 2001) and Bennett et al. [U.S. Patent No: 6,214,986], (made of record in the previous Office Action mailed July 26, 2004). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed August 22, 2007.

Response to Arguments

In response to this rejection, Applicants argue that none of Webb, Waters, or Bennett, alone or in combination, suggests a cycle of therapy as short as 3 to 9 days, as recited in the present claims. Applicants argue that as explained in the Novick Declaration filed April 30, 2007, neither Webb nor Waters teaches or suggests changing the treatment regiment to anything shorter than a two-week course of therapy. This argument has been fully considered, but is not found persuasive because KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396).

Furthermore, the Examiner did not rely on either Webb or Waters (*per se*) to suggest shortening a cycle of therapy to 3 to 9 days. Instead, this motivation came from the explicit teachings of Bennett et al. who taught that, regarding antisense oligonucleotide therapy, persons of ordinary skill in the art can easily [emphasis added] determine repetition rates. Therefore, it is the Examiner's position that Webb, Water, and Bennett in combination suggests Applicant's claimed invention.

Applicants next argue that Bennett does not cure the deficiencies of Webb and Waters because Bennett is not directed to the administration of bcl-2 oligonucleotides and thus would be viewed by one of ordinary skill in the art as being less pertinent that the disclosures of Webb and Waters. This argument has been fully considered, but is not found persuasive because regarding antisense therapy, it is well known in the art to

vary the cycles of therapy to determine optimal therapeutic benefit. This is best demonstrated by Bennett et al. who teaches that regarding antisense therapy, persons of ordinary skill can easily determine repetition rates of antisense oligonucleotides. Specifically, Bennett teaches, “[T]he formulation of therapeutic compositions and their subsequent administration is believed to be within the skill of those in the art." Bennett also teach, "[D]osing is dependent on severity and responsiveness of the disease state to be treated, with the course of treatment lasting from several days to several months, or until a cure is effected or a diminution of the disease state is achieved.” Therefore, given these disclosures, it is the Examiner’s position that the teachings of Bennett would not be viewed by one of ordinary skill in the art as being impertinent.

Applicants next argue that the teachings of Bennett are so broad as to be essentially meaningless since it is not possible to derive a suggestion that the two-week cycle of therapy disclosed by Webb should be shortened to 3 to 9 days from a disclosure of treatment that ranges from daily to every 20 years. This argument has been considered, but is not found persuasive because as discussed *supra*, Bennett teach that persons of ordinary skill can easily [emphasis added] determine repetition rates of antisense oligonucleotides. Given this disclosure, it is quite clear that the administration of antisense oligonucleotides for the purpose of therapeutic treatment is believed to be within the skill of those in the art.

Applicants next argue that in the previous Office Action mailed August 22, 2007, at pages 5 and 6, the Examiner has misapplied the law in quoting M.P.E.P. §2112.01, *Best*, and *Spada* since both are directed to product claims and whether a prior art

disclosure inherently anticipates such product claims. Applicants contend that the present claims are method claims. Applicants also argue that what is at issue in this rejection is not anticipation, but obviousness. This argument has been fully considered, but is not found persuasive because Applicant is encouraged to revisit *In re Best*. Particularly, see *Best*, 562F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) (Applicant claimed a process for preparing a hydrolytically-stable zeolitic aluminosilicate which included a step of "cooling the steam zeolite ... at a rate sufficiently rapid that the cooled zeolite exhibits a X-ray diffraction pattern ...." All the process limitations were expressly disclosed by a U.S. patent to Hansford except the cooling step. The court stated that any sample of Hansford's zeolite would necessarily be cooled to facilitate subsequent handling. Therefore, a *prima facie* case under 35 U.S.C. 102/103 was made. Applicant had failed to introduce any evidence comparing X-ray diffraction patterns showing a difference in cooling rate between the claimed process and that of Hansford or any data showing that the process of Hansford would result in a product with a different X-ray diffraction. Either type of evidence would have rebutted the *prima facie* case under 35 U.S.C. 102. A further analysis would be necessary to determine if the process was unobvious under 35 U.S.C. 103).

Applicants next argue that the Examiner is using the supposedly inherent treatment of cancer in Patient 6 as motivation to shorten treatment cycles and arrive at the presently claimed limitation of shortened cycles of therapy comprising 3 to 9 days. Applicants contend that this is an improper use of the concept of inherency since an inherent characteristic may not be used as motivation to make changes in the prior art.

Applicants specifically argue that an unknown property cannot motivate one to make an invention that depends on the unknown property. These arguments and contentions have been fully considered but are not found persuasive because first, inherency was not used as motivation to make changes in the prior art. Second, the Examiner is not sure what Applicant is arguing is an "unknown property".

For example, it is known that bcl-2 antisense can be used to treat cancer (see Webb et al.). It is also known that in Patient 6, at week 1 and week 2, bcl-2 protein levels were decreased (see Webb et al. Figure 2). It is also known that in Patient 6, at week 2, tumor reduction is observed (see Webb et al. Table 3). What is not known is whether Patient 6 exhibited tumor reduction as early as week 1. Webb et al. are silent as to this observation.

The primary issue at hand is that the claims of the instant invention are drawn to “A method of treating cancer in a human”. Now then, referring to Applicant’s specification, at page 6, forth paragraph, Applicants disclose, “[A]s used herein, the phrases “treating cancer” and "treatment of cancer” mean to… decrease tumor size”. Given this disclosure, it is quite clear that inherency was not used as motivation to make changes in the prior art since Webb et al. clearly teach that Patient 6, at week 2, exhibited tumor shrinkage (see Table 3). While the Examiner agrees that Webb et al. are silent as to whether or not Patient 6 exhibited tumor reduction as early as week 1, the burden was shifted to Applicant to provide evidence that this was not the case. In the form of evidence, Applicants provided the Novick Declaration which was of the opinion that Patient 6 did not show a “Promising cancer response” (see page 12).

However, this is not persuasive because according to Applicant's definition of "treating cancer", it is the Examiner's position that the results of Webb et al. were very promising.

Furthermore, regarding Applicant's arguments that the Examiner used the inherent treatment of cancer in Patient 6 as motivation to shorten treatment cycles and arrive at the presently claimed limitation of shortened cycles of therapy to 3 to 9 days, this is not found persuasive because as discussed *supra*, it is known that in Patient 6, at week 1 and week 2, bcl-2 protein levels were decreased (see Webb et al. Figure 2). It is also known that in Patient 6, at week 2, tumor shrinkage is observed (see Webb et al. Table 3). Given Applicant's definition of "treating cancer" coupled with *In re Best*, and the teachings of Bennett et al. that persons of ordinary skill in the art can easily determine repetition rates of antisense oligonucleotides, it is the Examiner's position that one of ordinary skill in the art would have been motivated to take the combined teachings of Webb et al. and Bennett et al. to arrive at Applicant's claimed invention, namely shortened treatment cycles of therapy to 3 to 9 days.

Applicants next argue that the Examiner's inherency argument is untenable because there is no evidence to support the position that Patient 6's cancer was treated at 1 week. Applicants contend that Patient 6 received the full, two-week course of therapy and therefore, any improvement in the condition of patient 6 can only be attributed to that full, two-week course of therapy. Applicants argue that it is irrelevant for this obviousness inquiry that Patient 6's bcl-2 levels may have been reduced after 1 week, since nothing ties that 1 week of treatment to any success in treating cancer. In this regard, Applicants argue that the assumption that Patient 6's cancer was inherently

treated at day 7 lacks any evidentiary basis. These arguments and contention have been fully considered, but are not found persuasive. It is the Examiner's position that the fact that at week 1 and week 2, bcl-2 levels were decreased in Patient 6, and at week 2, Patient 6 showed cancer treatment (e.g. tumor reduction), it is relevant to know whether, at week 1, Patient 6 exhibited tumor shrinkage. In determining this relevancy, the Examiner shifted the burden to Applicant to provide evidence that at week 1, Patient 6 did not show signs of cancer treatment (e.g. tumor shrinkage). In meeting this burden, Applicants provided the opinionated Novick Declaration which argued that, "One would not know whether the total infusion of 14 days was necessary to provide treatment of cancer or whether infusion of 7 days of therapy would be sufficient". It is noted that in relying on *In re Best*, this is exactly what the Examiner wants Applicants to prove. Therefore, since Webb et al. do not explicitly say that at week 1, Patient 6 exhibited cancer treatment (e.g. tumor reduction), and furthermore, since Webb et al. are silent as to the tumor response at week 1, the burden has been shifted to Applicants to provide evidence of Patient 6's tumor response at week 1.

Applicant is reminded that the Patent Office is not a research facility. See *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) at MPEP 2112. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not."

Furthermore, the mere fact that Webb et al. observed that similar to week 2, Patient 6's bcl-2 protein levels were decreased as early as week 1 lends full evidentiary

basis to know whether similar to week 2, if Patient 6 exhibited cancer treatment (e.g. tumor shrinkage) at week 1, as well.

Applicants next argue that according to the Novick Declaration, “Patient 6 did not show a promising cancer treatment" since only near partial responses were observed. Applicants contend that, according to the Novick Declaration, Webb et al. actually teach away from the present invention since the results were “not impressive". Applicants contend that based on the Novick Declaration, if anything, Webb et al. suggest that the cycles of therapy should be lengthened beyond the 2 week cycles of therapy taught therein since the results were "not impressive". Applicant's assertions have been fully considered, but are not found persuasive because as discussed *supra*, the issue at hand is that the claims of the instant invention are drawn to “A method of treating cancer in a human”. Now then, referring to Applicant’s specification, at page 6, forth paragraph, Applicants disclose, “[A]s used herein, the phrases “treating cancer” and "treatment of cancer” mean to… decrease tumor size”. Given Applicant’s definition, it is quite clear that, contrary to Applicants assertions, Patient 6 did indeed show promising cancer treatment (e.g. tumor reduction). Furthermore, it is quite evident that the results of Patient 6 were quite impressive as well.

Regarding Applicant's assertions that Webb et al. teach away from the present invention, this is not found persuasive because it is the Examiner's position that the teachings of Webb et al. are hardly a teaching away from the present invention. As discussed *supra*, it is known that in Patient 6, at week 1 and week 2, bcl-2 protein levels were decreased (see Webb et al. Figure 2). It is also known that in Patient 6, at week 2,

tumor shrinkage is observed (see Webb et al. Table 3). Given Applicant's definition of "treating cancer" coupled with *In re Best*, and the teachings of Bennett et al. that persons of ordinary skill in the art can easily determine repetition rates of antisense oligonucleotides, it is the Examiner's position that one of ordinary skill in the art would have been motivated to take the combined teachings of Webb et al. and Bennett et al. to arrive at Applicant's claimed invention, namely shortened treatment cycles of therapy comprising 3 to 9 days.

Applicants finally argue that Webb et al. do not teach the same steps as presently claimed since the present claims require more than one cycle of 3 to 9 days, separated by an interval of at least one day. Applicants contend that Webb teaches only a two-week treatment period. This argument and contention have been fully considered, but are not found persuasive. Applicant is reminded that the test for obviousness is not whether the features of the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375. Applicant argues against the Webb et al. reference individually, but must consider the rejection based upon the combination of the references. See MPEP 2145. When taken the Webb et al. reference in combination with the teachings of Bennett et al., who teach that persons of ordinary skill in the art can easily [emphasis added] determine repetition rates of antisense oligonucleotides, it

is the Examiner's position that in totality these teachings render the instant claims obvious.

In view of the foregoing, when all the evidence is considered, the totality of the rebuttal evidence of non-obviousness fails to outweigh the evidence of obviousness made of record. Thus, it is maintained that the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
March 14, 2008

/Sean R McGarry/

Primary Examiner, Art Unit 1635

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	09/709,170	WARRELL ET AL.	
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